Invasive Amoebiasis in Two Patients with AIDS and Cytomegalovirus Colitis

GERD FÄTKENHEUER,1* GEORG ARNOLD,2 HANS-MICHAEL STEFFEN,3 CASPAR FRANZEN,1 MATTHIAS SCHRAPPE,4 VOLKER DIEHL,1 AND BERND SALZBERGER1

Departments of Internal Medicine 1 and IV,2 Institute of Pathology,3 and Quality Management,4 University of Cologne, 50924 Cologne, Germany

Received 5 February 1997/Returned for modification 4 March 1997/Accepted 30 April 1997

Homosexual persons or human immunodeficiency virus (HIV)-infected patients frequently excrete cysts of nonpathogenic strains of Entamoeba histolytica (“Entamoeba dispar”). However, invasive amoebiasis is rare. We report two patients with AIDS and cytomegalovirus colitis in whom invasive amoebiasis was histologically diagnosed. It is concluded that E. histolytica has to be considered in HIV-infected patients with colitis.

The differential diagnosis of chronic diarrhea in patients with human immunodeficiency virus (HIV) infection is very broad and includes bacterial (Salmonella species, Shigella species, Yersinia species, and mycobacterium), viral (cytomegalovirus [CMV], herpes simplex virus, adenovirus), and parasitic (Cryptosporidium and microsporidium) infections (10, 20). Thorough diagnostic work-up leads to the identification of a pathogen in a high percentage (17), and multiple infections are common in AIDS patients (3).

Although amoebic cysts are frequently found in the stools of homosexual individuals, invasive amoebiasis has been very rarely observed in HIV-infected patients. Therefore, amoebiasis has not been included in the Centers for Disease Control and Prevention case definition of AIDS (6, 7) as an AIDS-defining event.

Here, we report two cases of invasive amoebiasis in AIDS patients with CMV colitis.

Patient 1. This bisexual man, born in 1956, was first diagnosed as HIV infected in November 1989. Beginning in March 1991, he complained of abdominal symptoms, with watery diarrhea and cramps. Repeated stool cultures were negative for bacteria and viruses. Stool examinations for parasites had not been done at that time. Consecutive colonoscopies showed nonspecific inflammation and CMV colitis, respectively, but no signs of other infections were present.

In June 1991, the patient was treated with ganciclovir for 3 weeks. Two months after the successful treatment of CMV colitis, the patient had a recurrence of bloody diarrhea. In October 1991, a relapse of CMV colitis was diagnosed clinically, because the patient was not willing to undergo repeat colonoscopy. Neither wet mounts nor concentration examinations were performed, since parasites had not been considered as potential pathogens by the treating physician. A 4-week course of foscarnet therapy failed to improve the patient’s symptoms. Colonoscopy then revealed severe hemorrhagic and ulcerating colitis. Histologically, no signs of CMV colitis were present. Instead, invasive amoebiasis could be demonstrated by the presence of erythrophagac trophozoites in the debris of a mucosal ulcer. Additionally, wet mounts of fresh stools revealed erythrocytophagocytic trophozoites of Entamoeba histo-

lytica. A serologic immune fluorescence test for amoebae was negative.

Foscarnet therapy was stopped in November 1991, and the patient was treated with metronidazole (750 mg three times a day [TID] for 10 days), resulting in an immediate reduction of diarrhea. However, 3 weeks later he had another episode of dysentery. Trophozoites of E. histolytica were again present in the stool samples. Treatment with metronidazole was repeated and followed by diloxanide (500 mg TID for 10 days). No further episode of amoebiasis or CMV colitis was observed until the patient’s death in May 1995.

Patient 2. This homosexual man, born in 1951, was diagnosed with HIV infection in December 1991. Beginning in August 1993, he had watery diarrhea. Repeated stool examinations for bacteria and parasites following concentration were negative. In October 1993, ulcerating colitis was diagnosed by colonoscopy. Histologically, CMV infection could be demonstrated. Additionally, amoebic colitis was diagnosed histologically by demonstration of ulcers with erythrophagac trophozoites in the exudate. The patient was treated in another hospital with ganciclovir for 3 weeks, resulting in an incomplete resolution of diarrhea. Information is not available on why he was not treated for amoebiasis.

Repeat colonoscopy in November 1993 showed progressive ulcerative colitis. Biopsies revealed no signs of CMV colitis but again demonstrated invasive amoebiasis. A serologic test for amoebiasis and stool examinations for amoeba had not been performed. Treatment with metronidazole (750 mg TID) and paromomycin (250 mg four times a day) for 14 days led to a complete resolution of diarrhea.

In January 1994, the patient presented with recurrent diarrhea. Colonoscopy showed ulcerating colitis, and histology exhibited CMV colitis. No signs of amoebic disease could be detected histologically, and on examination of a fresh unstained stool sample, no trophozoites were found. The patient improved with ganciclovir therapy and had no recurrent diarrhea until his death in November 1994.

In the two HIV-infected patients discussed above, invasive amoebiasis was diagnosed by biopsy. The diagnosis was established by the histological demonstration of erythrophagac amoebic trophozoites in fibrinous and granulocytic exudate from ulcers. A direct mount of fresh stools had only been performed for one patient before initiation of antiamoebic therapy, and it was positive. Besides amoebiasis, CMV colitis was diagnosed for both persons by the histological demonstration of multiple inclusion bodies. The patients showed resolu-
tion of diarrhea only after completing antiparasitic chemotherapy, further demonstrating the clinical significance of amoebiasis.

Cysts of *E. histolytica* have been reported to occur in up to 25% of AIDS patients with diarrhea (17) and in 37% of homosexual persons attending a sexually transmitted disease clinic (12). However, this parasite occurs in homosexual men as a commensal rather than a pathogenic organism. Allason-Jones and coworkers were able to demonstrate that all isolates in their series belonged to nonpathogenic strains of *E. histolytica* (2). Similarly, Burchard et al. characterized all strains from 20 HIV-infected patients with excretion of *E. histolytica* as nonpathogenic (5).

The discrepancy between the frequent detection of amoebic cysts and the absence of clinical disease in homosexual men and in HIV-infected individuals underlines the concept of two morphologically identical but pathogenetically different strains of *E. histolytica*. There is overwhelming evidence from biochemical, immunological, and genetic data that a potentially pathogenic strain of *E. histolytica* (Schaudinn) can be differentiated from a nonpathogenic strain (*Entamoeba dispar* Brumpt) (8). Because amoebae in homosexual and HIV-infected persons generally are nonpathogenic, the detection of cysts in stool samples of these patients does not necessitate antiparasitic therapy (1, 15).

Even in regions with high incidences of amoebiasis, invasive disease is very rare in HIV-infected individuals (11). There is a striking discrepancy in the incidence of invasive amoebiasis between HIV-infected and noninfected African people (9). However, under other conditions of immunosuppression, such as steroid therapy or malnutrition, invasive amoebiasis is more frequent and more severe (13).

Only a few cases of invasive amoebiasis in homosexual men or in HIV-infected individuals have been reported in the literature. In an autopsy series of 94 Mexican patients diagnosed with AIDS, one person with amoebic colitis was found (15). Blanshard et al. reported an AIDS patient who died from severe enterocolitis and peritonitis. While stool examinations for pathogens, including amoebae, were negative, a rectal biopsy showed histologic evidence for invasive amoebiasis (4). A third patient was reported from Japan (14). An English hemophilic patient with HIV infection, amoebic dysentery, and a subsequent diagnosis of ulcerative colitis has also been reported in the literature (19). However, no definitive evidence for the diagnosis of invasive amoebiasis in that patient was given (19), and the diarrhea may have been due to preexisting ulcerative colitis. Finally, there are two reports of homosexual patients with established diagnoses of invasive amoebic disease. HIV infection had been ruled out for one patient (18), and the status of HIV infection was not reported for the other (16).

Both patients reported in our study had no travel history to subtropical or tropical areas, a major risk factor for the acquisition of amoebiasis, so they must have acquired *E. histolytica* infection in Middle Europe. Serology was done for one patient and was negative. This may be explained by the severe immunosuppression of the patient.

In conclusion, amoebiasis has to be considered in the differential diagnosis of HIV-infected patients with diarrhea. An examination of stools for amoebic trophozoites is recommended for patients with bloody diarrhea. Colonoscopy with histological examination is the most reliable examination to establish a definite diagnosis of invasive infection with *E. histolytica*.

We are indebted to Hanns Martin Seitz (Institute of Medical Parasitology, University of Bonn, Germany) for his valuable advice during the preparation of the manuscript.

REFERENCES